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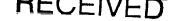
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				ation Number	09/601,490					
STA	LEM	ENT	BY A	PPL	CANT		Filing C	amed Inventor	September 21, 2000 Désiré José COLLEN	
				Art Unit	1652	<u> </u>				
	(use as many sheets as necessary)				ner Name	Delia M. Ramirez				
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¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

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## PADEMBALULE for form 1449A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 4 of

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Complete	Complete if Known							
Application Number	09/601,490							
Filing Date	September 21, 2000							
First Named Inventor	Désiré José COLLEN							
Group Art Unit	1652							
Examiner Name	Delia M. Ramirez							
Attorney Docket Number	702-001463							

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, cite and/or country where published.	T²
7012	BE	COLLEN, D. et al. "Isolation and Characterisation of Natural and Recombinant Staphylokinase" Fibrinolysis 6: 203-213 (1992)	
<i>,</i>	BF	COLLEN, D. et al. "Comparative Thrombolytic and Immunogenic Properties of Staphylokinase and Streptokinase" Fibrinolysis 6: 232-242 (1992)	
	BG	BIAcore Methods Manual "Immobilization" pp: 5-2 through 5-4, Pharmacia Biosensor AB, Uppsala, Sweden	
	вн	Gibaldi, M. et al. "Pharmacokinetics" 2 nd Ed. Marcel Dekker Inc., New York, N.Y. pp: 45-111 (1983)	
	ВІ	INADA, Y. et al. "Biomedical and Biotechnological Applications of PEG- and PM-modified Proteins" Tibtech 13: 86-91 (1995)	
	BJ	RABIJNS, A. et al. "Three-dimensional Structure of Staphylokinase, a Plasminogen activator with Therapeutic Potential" <i>Nature Structural Biology</i> 4(5): 357-360 (1997)	
DR	BK	JESPERS, S. et al. "Structural and Functional Basis of Plasminogen Activation by Staphylokinase" Thromb Haemost 81: 479-485 (1999)	

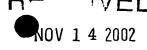
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Substitute for form	n 1449A/PTO						
				Complete if Known			
INFORM	MATION D	NSCLOS	URE	Application Number	09/601,490		
STATEMENT BY APPLICANT			ΔΝΤ	Filing Date	September 21, 2000		
				First Named Inventor	Désiré José COLLEN		
(use as many sheets as necessary)				Group Art Unit	1652		
				Examiner Name	Delia M. Ramirez		
Sheet	2	of	4	Attorney Docket Number	702-001463		

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, cite and/or country where published.	T²
on	AC	LACK, C.H. "Staphylokinase: an Activator of Plasma Protease" Nature 161: 559-560 (1948)	
	AD	LEWIS, J.H. et al. "A Proteolytic Enzyme System of the Blood. III. Activation of Dog Serum Profibrinolysin by Staphlokinase" Am J Physiol 166: 594-602 (1951)	
	AE	VANDERSCHUEREN, S. et al. "A Randomized Trial of Recombinant Staphylokinase Versus Alteplase for Coronary Artery Patency in Acute Myocardial Infarction" Circulation 92(8): 2044-2049 (1995)	
	AF	SAKO, T. et al. "Cloning and Expression of the Staphylokinase Gene of Staphylococcus aureus in Escherichia coli" Mol Gen Genet 190: 271-277 (1983)	
	AG	BEHNKE, D. et al. "Cloning and expression in <i>Escherichia coli, Bacillus subtilis</i> , and <i>Streptococcus sanguis</i> of a gene for staphylokinase – a bacterial plasminogen activator" <i>Mol Gen Genet</i> <b>210</b> : 528-534 (1987)	
	AH	SAKO, T. et al. "Nucleotide sequence of the staphylokinase gene from Staphylococcus aureus" Nucleic Acids Research 11(22): 7679-7683 (1983)	
	Al	SAKAI, M. et al. "Mechanism of Fibrin-Specific Fibrinolysis by Staphylokinase: Participation of α ₂ -Plasmin Inhibitor" <i>Biochem Biophys Res Comm</i> <b>162</b> (2): 830-837 (1989)	
	AJ	MATSUO, O. et al. "Thrombolytic Properties of Staphylokinase" Blood 76(5): 925-929 (1990)	
	AK	LIJNEN, H.R. et al. "On the Mechanism of Fibrin-specific Plasminogen Activation by Staphylokinase" J Biol Chem 266(18): 11826-11832 (1991)	
	AL	LIJNEN, H.R. et al. "On the molecular interactions between plasminogen-staphylokinasse, α ₂ -antiplasmin and fibrin" <i>Biochim Biophys Acta</i> <b>1118</b> : 144-148 (1992)	
	AM	SILENCE, K. et al. "Interaction between Staphylokinase, Plasmin(ogen), and α ₂ -Antiplasmin" <i>J Biol Chem</i> <b>268</b> (13): 9811-9816 (1993)	
	AN	SILENCE, K. et al. "Regulation by α ₂ -Antiplasmin and Fibrin of the Activation of Plasminogen with Recombinant Staphylokinase in Plasma" <i>Blood</i> <b>82</b> (4): 1175-1183 (1993)	
1	AO	SAKHAROV, D.V. et al. "Interactions between Staphylokinase, Plasmin(ogen), and Fibrin" J Bio Chem 271(44): 27912-27918 (1996)	
DR	AP	SCHLOTT, B. et al. "Staphylokinase Requires NH ₂ -terminal Proteolysis for Plasminogen Activation" J Bio Chem 272(9): 6067-6072 (1997)	

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INFORM	MATION D	DISCLOS	URE	Application Number	09/601,490	7		
STATE	MENT BY	APPLICA	ΔΝΤ	Filing Date	September 21, 2000	3		
OTATEMENT DI ALI LICANI				First Named Inventor	Désiré José COLLEN	=		
(use as many sheets as necessary)				Group Art Unit	1652			
				Examiner Name	Delia M. Ramirez			
Sheet	3	of	4	Attorney Docket Number	702-001463	8		

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	<u>7</u>			
Examiner Initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, cite and/or country where published.	0/240¢			
DR	AQ	COLLEN, D. et al. "Comparative Immunogenicity and Thrombolytic Properties Toward Arterial and Venous Thrombi of Streptokinase and Recombinant Staphylokinase in Baboons" <i>Circulation</i> <b>87</b> (3): 996-1006 (1993)				
4	AR	WHITE, H. "Thrombolytic treatment for recurrent myocardial infarction" Br Med J 302: 429-430 (1991)				
	AS	GASE, A. et al. "Functional Significance of NH ₂ - and COOH-Terminal Regions of Staphylokinase in Plasminogen Activation" <i>Thromb Haemost</i> <b>76</b> (5): 755-760 (1996)				
	AT	SCHLOTT, B. et al. "High Yield Production and Purification of Recombinant Staphylokinase for Thrombolytic Therapy" <i>Bio/Technology</i> 12: 185-189 (1994)				
	AU	HORTON, R.M. et al. "Engineering hybrid genes without the use of restriction enzymes: gene splicing by overlap extension" <i>Gene</i> 77: 61-68 (1989)				
	AV	KARLSSON, R. et al. "Kinetic analysis of monoclonal antibody-antigen interactions with a new biosensor based analytical system" J Immunol Methods 145: 229-240 (1991)				
	AW	BRADFORD, M.M. "A Rapid and Sensitive Method for the Quantitation of Microgram Quantities of Protein Utilizing the Principle of Protein-Dye Binding" <i>Anal Biochem</i> 72: 248-254 (1976)				
	AX	DEUTSCH, D.G. et al. "Plasminogen: Purification from Human Plasma by Affinity Chromatography" Science 170: 1095-1096 (1970)				
	AY	VANDERSCHUEREN, S. et al. "Thrombolytic Therapy of Peripheral Arterial Occlusion with Recombinant Staphylokinase" Circulation 92(8): 2050-2057 (1995)				
	AZ	COLLEN, D. et al. "Thrombolytic Properties of Poorly Immunogenic Variants of Recombinant Staphylokinase" Fibrinolysis & Proteolysis 12(Suppl. 1): 30 (1998)				
	ВА	COLLEN, D. et al. "Recombinant Staphylokinase Variants with Altered Immunoreactivity. III: Species Variability of Antibody Binding Patterns" Circulation 95(2): 455-562 (1997)				
	BB	COLLEN, D. et al. "Recombinant Staphylokinase Variants with Altered Immunoreactivity. IV: Identification of Variants with Reduced Antibody Induction but Intact Potency" Circulation 95(2): 463-472 (1997)				
	ВС	COLLEN, D. et al. "Recombinant Staphylokinase Variants with Altered Immunoreactivity I: Construction and Characterization" Circulation 94(2): 197-206 (1996)				
TOP	BD	COLLEN, D. et al. "Recombinant Staphylokinase Variants with Altered Immunoreactivity. II: Thrombotic Properties and Antibody Induction" <i>Circulation</i> 94(2): 207-216 (1996)				

	Examiner Signature	Date Considered	1/	129/03
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